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Dockets Management Branch (HFA-305)
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

Re: Draft Guidance on Placing the FDA Therapeutic Equivalence Code on Prescription Drug Labels and Labeling
Docket No. 98D-1266; 64 Fed. Reg. 4434 (Jan. 28, 1999)

Dear Sir or Madam:

Bristol-Myers Squibb Company (BMS) is a diversified worldwide health and personal care company with principal businesses in pharmaceuticals, consumer medicines, beauty care, nutritionals and medical devices. We are a leading company in the development of innovative therapies for cardiovascular, metabolic, oncology, infectious diseases, and neurological disorders. BMS is committed to the use of labels and labeling in the marketing of prescription drugs that are fully informative and not misleading.

For these reasons, BMS is very interested in the draft guidance for industry that the Food and Drug Administration (FDA) made available on January 28, 1999, regarding the use in prescription drug labeling of the therapeutic rating system established in the FDA Orange Book. BMS does not believe that this draft guidance advances the FDA's goal of clearly communicating the critical information health care professionals and consumers must have in order to safely and effectively use prescription drugs.

The draft guidance would allow a generic drug company to place, in its label or labeling, a claim setting forth the therapeutic rating of its generic drug in relationship to the pioneer drug, as identified by its trademark. For example, a generic drug would be allowed to state: "AB to pioneer trademark." For the reasons set forth below, the proposed new policy set forth in the draft guidance is defective as a matter both of policy and of law. It, therefore, could never have been implemented by regulation under the Administrative Procedures Act. The FDA cannot recommend, through the issuance of guidances, actions that the agency is precluded from permitting by regulation. Therefore, BMS respectfully urges the FDA to withdraw this draft guidance.

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The FDA's stated objectives for proposing the new draft guidance are to facilitate accurate and safe selection of drug products by health care practitioners and state health officials. Instead, by creating a perception that all of the relevant therapeutic equivalence language is summarized on the product label, this guidance will confuse and mislead both health professionals and consumers, and is likely to contribute to inaccurate and unsafe selection of drug products.

The FDA, instead, should be directing everyone desiring such information to refer to the Orange Book, which is readily available to professionals and consumers alike in both print and electronic versions. As the draft guidance points out, the Orange Book information is "dynamic and complex and is subject to changing conditions" (page 6). Reviewing individual product labels, which may contain out-of-date information and in any event show only one product at a time, is of little or no help to health care practitioners.

Furthermore, FDA would be faced with new and unnecessary enforcement obligations: (a) to monitor and determine that therapeutic equivalence information on a label remains correct, and (b) to require the withdrawal of a product determined to contain incorrect information on its label. Most likely, the FDA will receive complaints regarding generic labels that fail to keep up with Orange Book-listed new indications for, and dosage forms of, the pioneer version.

Use of the pioneer trademark in generic drug labeling, as proposed by the draft guidance, violates several sections of the Federal Food, Drug, and Cosmetic Act: 502(a), against mislabeling; 502(l)(2) and (3), against imitations offered for sale under another drugs name; and 505(j)(2)(A)(v), requiring same labeling.

The draft guidance also encourages violation of federal trademark law, as set forth in the Lanham Act. The draft guidance encourages acts that constitute unlawful infringement under Section 32; unfair competition under Section 43; and unlawful dilution of a famous mark under Section 43.

Allowing use of the pioneer trademark in generic drug labeling, as proposed by the draft guidance, would also violate the Taking Clause of the Fifth Amendment to the United States Constitution. Trademarks are intellectual property and are, thus, clearly included in the definition of 'property' under the United States Constitution. As such, the granting under color of governmental action of a right to use such property to someone other than the owner requires compensation to the owner. No provision for compensation of innovator companies for use of their trademarks by generic companies is provided for in the draft guidance.

The draft guidance changes longstanding FDA statutory policy and establishes complex and extensive new regulatory rules for prescription drug labeling. Such changes may lawfully be promulgated only after notice-and-comment rulemaking in compliance with the Administrative Procedure Act – a step that has yet to be taken by the FDA.

Additionally, the implementation of this draft guidance would add a trademark to the generic drug's label for the first time, since most generic drugs do not have trademarks associated with them. The presence of an innovator's trademark on a generic's label, regardless of any restrictions on placement location or type size, will inevitably lead to the reporting of the generic's adverse events against the innovator's product. This will lessen the value of the information the FDA receives on drug products and could potentially delay action the FDA would otherwise take to protect the public.

FDA cannot *recommend* actions which it is precluded by law from *authorizing*. Section 202 of the Drug Amendments Act of 1962 precludes the FDA from invalidating any provision of state law. Approximately 12 states currently maintain their own formularies under which generic substitution is controlled. The therapeutic equivalence statement allowed under the draft guidance would be silent as to statutory basis for making the claim. This will create confusion in those states in which state formularies, and not the Orange Book, are the final determiners of substitutability. Placing Orange Book-derived therapeutic equivalence information on a generic label will tempt time-pressured pharmacists to accept the statement, rather than referring to their state-mandated formulary. The only logical response by such states – to require labels to state, "X is AB to pioneer trademark *except in States U, Y and Z*" -- is most likely unachievable under the supremacy doctrine of the Constitution. This result means the draft guidance invalidates state law, thus violating Section 202 of the Drug Amendments of 1962.

The FDA indicates that this draft guidance is authorized by the recent repeal of Section 301(l) of the FD&C Act. (That Section prohibited the use, in the labeling of a drug, of any statement that an NDA had been approved for the drug or that the drug otherwise complies with Section 505). Section 301(1) was repealed in order to allow accurate and truthful statements that the FDA has approved an NDA or an ANDA. There is no suggestion in the repeal of this provision or in the legislative history that it was in any way intended to permit generic drug labeling to refer to pioneer trademarks.

Finally, the draft guidance violates the balance between generic and pioneer drugs established under the Drug Price Competition and Patent Term Restoration Act of 1984 (the 1984 Act). If implemented as written, the draft guidance will allow generic companies to use pioneer companies' trademarks – trademarks that were developed by the pioneer companies only through large expenditures of marketing funds. This type of exchange of goodwill is neither contemplated, nor accounted for, in the 1984 Act. Furthermore, the balance between generic and pioneer drugs maintained through the requirement to establish bioequivalence is disrupted by the draft guidance. The requirement of bioequivalence applies not only between pioneer and generic versions of a drug, but also between dosage forms and strengths: capsules are not equivalent to tablets, injectables are not equivalent to orals, aqueous solutions are not equivalent to dry powder, immediate release tablets are not equivalent to extended release tablets, and, until proven through testing, two 15 mg tablets are not equivalent to one 30 mg tablet. By allowing the use of "AB to

pioneer trademark", without requiring any limitation as to dosage form, strength, or indication, the draft guidance creates the impression that generic drug products have 'across-the-board' equivalence to all dosage forms, strengths and indications of the innovator's trademarked product. Such presumptions were not part of the 1984 Act.

In conclusion, the draft guidance would (a) abridge legal rights under two federal statutes and the United States Constitution, (b) reverse a longstanding FDA interpretation of the FD&C Act, (c) violate existing FDA regulations, and (d) establish entirely new labeling rules for generic drugs. BMS respectfully requests that the FDA consider whether or not the draft guidance is unlawful and cannot properly be pursued. If after thoughtful re-examination of the draft guidance, however, the FDA nonetheless wishes to pursue the expressed objectives of the guidance, at the very least the draft guidance must be subjected to notice-and-comment rulemaking in compliance with the Administrative Procedure Act.

Bristol-Myers Squibb Company appreciates this opportunity to provide comments on this draft guidance, and respectfully requests that the FDA give consideration to its recommendations. The undersigned would be pleased to provide additional pertinent information, as may be desired or requested by the Food and Drug Administration.

Sincerely,

David T. Bonk

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